Leg length, insulin resistance, and coronary heart disease risk: The Caerphilly Study

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Abstract

***Background*—Adult height has been inversely associated with coronary heart disease risk in several studies. The mechanism for this association is not well understood, however, and this was investigated by examining components of stature, cardiovascular disease risk factors and subsequent coronary heart disease in a prospective study.**

***Methods*—All men aged 45–59 years living in the town of Caerphilly, South Wales were approached, and 2512 (89%) responded and underwent a detailed examination, which included measurement of height and sitting height (from which an estimate of leg length was derived). Participants were followed up through repeat examinations and the cumulative incidence of coronary heart disease—both fatal and non-fatal—over a 15 year follow up period is the end point in this report.**

***Results*—Cross sectional associations between cardiovascular risk factors and components of stature (total height, leg length and trunk length) demonstrated that factors related to the insulin resistance syndrome—the homeostasis model assessment of insulin resistance, fasting triglyceride levels and total to HDL cholesterol ratio—were less favourable in men with shorter legs, while showing reverse or no associations with trunk length. Fibrinogen levels were inversely associated with leg length and showed a weaker association with trunk length. Forced expiratory volume in one second was unrelated to leg length but strongly positively associated to trunk length. Other risk factors showed little association with components of stature. The risk of coronary heart disease was inversely related to leg length but showed little association with trunk length.**

***Conclusion*—Leg length is the component of stature related to insulin resistance and coronary heart disease risk. As leg length is unrelated to lung function measures it is unlikely that these can explain the association in this cohort. Factors that influence leg length in adulthood—including nutrition, other influences on growth in early life, genetic and epigenetic influences—merit further investigation in this regard. The reported associations suggest that pre-adult influences are important in the aetiology of coronary heart disease and insulin resistance.**

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Height in adulthood has been found to be inversely related to coronary heart disease (CHD) risk in various cohort studies.[1–6] As favourable socioeconomic circumstances are associated with greater height, the relation between height and CHD incidence may be confounded by the effects of childhood and adulthood socioeconomic conditions. While this seems to be partly the case, associations persist after adjustment for socioeconomic circumstances during adult life,[6 7] childhood[3] and both simultaneously.[8] Birth weight, which is associated with both height[9] and CHD incidence[9 10] also fails to account for the relation between adulthood height and CHD risk.[4 11]

Several mechanisms have been suggested for the association between height and CHD risk. These include: fetal growth[12] and childhood nutrition,[13] which influence achieved stature and may have long term effects on CHD risk; genetic influences that determine height and health simultaneously[2]; the poorer lung function associated with shorter stature[14]; the lesser diameter of coronary vessels in people of shorter height[15]; and reverse causation, with poor health leading to both shrinkage and increased CHD risk in adulthood.[16]

While it is likely that several of these factors may contribute to the association between height and CHD risk, one approach to further elucidating the relation is to analyse different components of height separately. It has been known for many years that the interruption of growth at any stage results in a relatively long torso and short legs.[17 18] If the rate of growth is sufficiently slowed down, for example by nutritional deficiency, the adult will have relatively short legs. Such proportions have been used as criteria for the study of nutrition and development in childhood, and have been investigated with respect to risk of cancer.[19 20] Recently leg length measured in childhood has been shown to be the component of stature most sensitive to environmental influences[21] and to demonstrate a strong inverse association with risk of CHD mortality over a 50 year follow up period.[13] In this paper we relate components of adult stature to CHD risk in a prospective study, which also allows for the examination of a wide range of potential underlying, confounding or mediating factors.

Methods

The Caerphilly study is based upon a 100% sample of men selected from the town of Caerphilly and five adjacent villages. The men were chosen by date of birth so that they were aged 45–59 years when examined between 1979 and 1983. A total of 2512 men were seen—89% of the 2818 who were found to be eligible. Full

Table 1 Pearson's correlation coefficients (and partial correlation coefficients controlling for age) for the correlations between height, trunk, leg length, leg length/trunk ratio and BMI

	Height	*Trunk length*	*Leg length*	*Leg:trunk ratio*	*BMI*
Height	1.00				
Trunk length	0.78 (0.78)	1.00			
Leg length	0.88 (0.88)	0.40 (0.39)	1.00		
Leg:trunk ratio	0.72 (0.73)	0.13 (0.13)	0.96 (0.96)	1.00	
BMI	−0.013 (−0.017)*	0.17 (0.16)	−0.14 (−0.15)	−0.20 (−0.20)	1.00

All correlations p<0.0001 except *, direct correlation p=0.53, partial correlation p=0.40.

details of screening and follow up procedures have been reported elsewhere.[4 22–24] Measurements included blood pressure, total and HDL cholesterol, triglycerides, insulin, glucose, fibrinogen, forced expiratory volume in one second (FEV_1), own and father's occupational social class, father's unemployment, own employment and smoking behaviour. Lung function was indexed by FEV_1/height squared[25] and insulin resistance was estimated according to the homeostasis model assessment (HOMA)[26] as the product of fasting glucose and insulin, divided by the constant 22.5. The higher the value, the greater the level of insulin resistance. These HOMA scores are available for only 2031 men because it was not assessed in diabetic men, those with a fasting blood glucose concentration $\geqslant$ 8 mmol per litre and participants with missing insulin or glucose measures.

Height was measured in millimetres using a Holtain stadiometer, with care being taken to ensure that the participant was standing upright with his back against the vertical stand, heels against the plate of the base and his chin down so that the middle of his ear was at the same horizontal level as his eyes. The participant was then asked to sit on a stool with his back against the vertical stand of the stadiometer and his sitting height was measured. For the purposes of these analyses leg length has been calculated by subtracting sitting height from standing height. While this contains the stool height—which was the same for each man but was not measured—this will not influence the quintiles or standard deviation of the measure. Height or sitting height were missing on 82 men and one man was a double amputee. Therefore the base sample for the following analyses is 2429 men.

The records of all men at the National Health Service Central Registry were flagged so that notification of death is automatic and a copy of the death certificate is received. Incident CHD was defined as in previous reports,[4 23 24] based on admission data to local hospitals, a questionnaire to men (whether still in the original area or having moved) regarding hospital admissions, hospital discharge letters from such admissions, and ECG recordings taken at follow up clinics held at five year intervals from the baseline measurements. The results recorded in this study refer to mortality follow up to the end of 1997 (between 14.25 and 18.25 years follow up) and for non-fatal CHD for an average of 13.75 years follow up.

Table 2 15 year age adjusted mortality and cumulative incidence of CHD per 100 men, according to different leg length, trunk length, height and leg to trunk length ratio quartiles, with standard errors (SE). P values based on continuous variables for stature, not quartiles

	1 - lowest quartile	*2*	*3*	*4 - highest quartile*	*p Value*
Leg length					
All deaths (639)	27.7 (1.8)	26.9 (1.8)	25.7 (1.8)	24.2 (1.7)	0.18
CHD deaths (263)	11.3 (1.3)	12.0 (1.3)	11.5 (1.3)	8.2 (1.1)	0.17
All incident CHD (435)	19.1 (1.6)	19.7 (1.6)	18.6 (1.6)	14.3 (1.4)	0.05
Trunk length					
All deaths (639)	25.8 (1.7)	28.9 (1.8)	25.8 (1.7)	24.7 (1.8)	0.82
CHD deaths (263)	9.9 (1.2)	12.0 (1.3)	11.2 (1.3)	10.3 (1.3)	0.49
All incident CHD (435)	16.6 (1.6)	19.9 (1.6)	18.2 (1.5)	17.2 (1.6)	0.40
Height					
All deaths (639)	26.0 (1.7)	28.4 (1.8)	25.2 (1.7)	24.9 (1.8)	0.30
CHD deaths (263)	10.1 (1.2)	12.4(1.3)	11.4 (1.3)	9.1 (1.2)	0.55
All incident CHD (435)	17.3 (1.5)	20.4 (1.6)	19.0 (1.5)	15.1 (1.5)	0.36
Leg length/trunk length ratio					
All deaths (639)	28.0 (1.7)	26.3 (1.7)	25.9 (1.8)	24.6 (1.7)	0.18
CHD deaths (263)	11.7 (1.3)	10.3 (1.2)	12.1 (1.3)	8.8 (1.2)	0.10
All incident CHD (435)	19.8 (1.6)	17.7 (1.6)	18.7 (1.5)	15.0 (1.5)	0.02

STATISTICAL METHODS

Pearson's correlation coefficients were calculated between the anthropometric variables. To illustrate the direction and shape of any associations between the four height variables—leg length, trunk length, total height and leg length to trunk length ratio—and other variables, quartiles were used. Age standardised means and prevalence of risk factors were determined for these quartiles. Age standardisation of prevalence was by the direct method in five 3 year age bands, 45–47, 48–50, 51–53, 54–56, and 57–59. Age standardisation of means was carried out with general linear modelling in the SAS procedure GLM. Statistical testing of possible associations was carried out using multiple regression, and using the continuous stature variables. Serum triglyceride and HOMA scores were found to be log normal, the geometric means have been quoted, and the natural log of the variables used in the regression models. Multiple logistic regression was used to explore the effects of other risk factors on the association between CHD and the height variables

Results

Inter-relations between the various anthropometric measures are presented in table 1. Several of these associations are consequences of variable construction—for example, the sizeable correlations between height and both leg and trunk length reflect the fact that the second are constituents of the first; while body mass index is a measure explicitly computed because of its lack of association with height. However, the relatively low correlation between leg length and trunk length reflect the importance of considering these components separately. Short legs are associated with higher body mass index, while the reverse is the case for trunk length. Men with a high leg to trunk length ratio have a lower body mass index than men with a low ratio.

Total mortality, coronary heart disease mortality and cumulative fatal and non-fatal incident coronary heart disease are displayed according to the anthropometric measures divided into quarters of their distributions in table 2. Longer legs are associated with lower coronary heart disease risk. Height and trunk length are not related to either fatal or total coronary heart disease rates after adjusting for age.

Cardiovascular disease risk factors and demographic data are presented according to quartiles of the anthropometric measures in

Table 3 Mean or prevalence and standard error (SE) of the mean or prevalence of age adjusted risk factors in men by leg length, sitting height, height and leg: trunk ratio quartiles. Age is the only variable not age adjusted

Variable	*1 - lowest quartile*	*2*	*3*	*4 - highest quartile*	*p Value for trend*
Leg length					
Age	52.5 (0.2)	52.5 (0.2)	51.9 (0.2)	51.4 (0.2)	0.0001
Systolic blood pressure (mm Hg)	141.8 (0.8)	139.9 (0.8)	140.8 (0.8)	140.6 (0.8)	0.43
Diastolic blood pressure (mm Hg)	90.0 (0.5)	88.0 (0.5)	88.4 (0.5)	88.3 (0.5)	0.19
Total cholesterol (mmol/l)	5.79 (0.05)	5.74 (0.05)	5.64 (0.05)	5.66 (0.05)	0.037
HDL cholesterol (mmol/l)	1.10 (0.01)	1.15 (0.01)	1.12 (0.01)	1.12 (0.01)	0.56
Total/HDL cholesterol	5.70 (0.08)	5.44 (0.08)	5.47 (0.08)	5.41 (0.08)	0.063
Triglyceride (mmol/l)*	1.82 (0.02)	1.66 (0.02)	1.65 (0.02)	1.62 (0.02)	0.0008
Fibrinogen (g/l)	3.81 (0.04)	3.81 (0.04)	3.76 (0.04)	3.69 (0.03)	0.004
FEV_1/height^2 (cl/m^2)	89.1 (1.0)	91.0 (1.0)	90.2 (1.0)	91.3 (0.9)	0.11
Insulin resistance* (HOMA)	1.43 (0.04)	1.24 (0.04)	1.26 (0.04)	1.22 (0.04)	0.013
Non-manual social class (%)	20.2 (1.7)	28.8 (1.9)	36.1 (2.0)	42.7 (2.0)	0.0001
Father in non-manual social class (%)	8.8 (1.2)	8.9 (1.2)	12.7 (1.4)	18.8 (1.6)	0.0001
Father unemployed (%)	50.4 (2.3)	49.5 (2.3)	46.4 (2.3)	36.2 (2.2)	0.0001
Subject employed at baseline (%)	75.2 (1.7)	78.9 (1.7)	81.3 (1.6)	85.9 (1.4)	0.0001
Ever smoker (%)	84.0 (1.5)	84.8 (1.5)	85.0 (1.4)	82.7 (1.5)	0.90
Trunk length					
Age	53.1 (0.2)	52.5 (0.2)	51.8 (0.2)	51.0 (0.2)	0.0001
Systolic blood pressure (mm Hg)	140.7 (0.8)	140.0 (0.8)	140.5 (0.8)	141.4 (0.8)	0.34
Diastolic blood pressure (mm Hg)	88.6 (0.5)	88.1 (0.5)	88.3 (0.5)	89.5 (0.5)	0.24
Total cholesterol (mmol/l)	5.75 (0.05)	5.80 (0.05)	5.67 (0.05)	5.64 (0.05)	0.016
HDL cholesterol (mmol/l)	1.16 (0.01)	1.13 (0.01)	1.12 (0.01)	1.08 (0.01)	0.0001
Total/HDL cholesterol	5.40 (0.09)	5.56 (0.08)	5.45 (0.08)	5.61 (0.09)	0.062
Triglyceride (mmol/l)*	1.66 (0.02)	1.69 (0.02)	1.65 (0.02)	1.76 (0.02)	0.055
Fibrinogen (g/l)	3.82 (0.04)	3.76 (0.04)	3.76 (0.03)	3.73 (0.04)	0.093
FEV_1/height^2 (cl/m^2)	86.2 (1.0)	90.1 (0.9)	91.4 (0.9)	93.5 (1.0)	0.0001
Insulin resistance* (HOMA)	1.23 (0.04)	1.24 (0.04)	1.26 (0.04)	1.45 (0.04)	0.0025
Non-manual social class (%)	24.3 (1.8)	29.5 (1.9)	31.7 (1.9)	43.7 (2.1)	0.0001
Father in non-manual social class (%)	11.0 (1.4)	11.4 (1.4)	13.1 (1.4)	14.4 (1.5)	0.006
Father unemployed (%)	47.8 (2.4)	47.8 (2.3)	43.9 (2.2)	42.1 (2.3)	0.0001
Subject employed at baseline (%)	76.5 (1.8)	79.5 (1.6)	81.3 (1.6)	82.8 (1.6)	0.012
Ever smoker (%)	85.9 (1.5)	84.1 (1.5)	82.5 (1.5)	84.3 (1.5)	0.22
Height					
Age	53.0 (0.2)	52.6 (0.2)	51.6 (0.2)	51.2 (0.2)	0.0001
Systolic blood pressure (mm Hg)	141.6 (0.8)	140.0 (0.8)	140.0 (0.8)	141.3 (0.8)	0.96
Diastolic blood pressure (mm Hg)	89.6 (0.5)	88.1 (0.5)	87.9 (0.5)	89.0 (0.5)	0.76
Total cholesterol (mmol/l)	5.74 (0.05)	5.78 (0.05)	5.69 (0.05)	5.64 (0.05)	0.008
HDL cholesterol (mmol/l)	1.14 (0.01)	1.13 (0.01)	1.11 (0.01)	1.11 (0.01)	0.047
Total/HDL cholesterol	5.47 (0.09)	5.55 (0.08)	5.57 (0.08)	5.45 (0.08)	0.75
Triglyceride (mmol/l)*	1.70 (0.02)	1.73 (0.02)	1.68 (0.02)	1.65 (0.02)	0.19
Fibrinogen (g/l)	3.77 (0.04)	3.81 (0.04)	3.79 (0.03)	3.69 (0.03)	0.005
FEV_1/height^2 (cl/m^2)	88.2 (1.0)	89.2 (1.0)	92.2 (1.0)	91.8 (0.9)	0.0001
Insulin resistance* (HOMA)	1.35 (0.04)	1.23 (0.04)	1.30 (0.04)	1.27 (0.04)	0.89
Non-manual social class (%)	20.1 (1.7)	28.9 (1.9)	35.8 (2.0)	43.1 (2.1)	0.0001
Father in non-manual social class (%)	7.7 (1.2)	11.9 (1.4)	13.8 (1.5)	16.0 (1.6)	0.0001
Father unemployed (%)	49.7 (2.4)	49.7 (2.3)	42.4 (2.3)	39.2 (2.2)	0.0001
Subject employed at baseline (%)	75.2 (1.8)	79.9 (1.6)	80.8 (1.6)	85.3 (1.5)	0.0001
Ever smoker (%)	82.7 (1.6)	85.7 (1.5)	83.9 (1.5)	83.7 (1.5)	0.47
Leg length/trunk length ratio					
Age	52.3 (0.2)	52.4 (0.2)	51.9 (0.2)	51.7 (0.2)	0.011
Systolic blood pressure (mm Hg)	141.7 (0.8)	140.3 (0.8)	141.0 (0.8)	140.2 (0.8)	0.27
Diastolic blood pressure (mm Hg)	90.1 (0.5)	88.0 (0.5)	88.3 (0.5)	88.2 (0.5)	0.074
Total cholesterol (mmol/l)	5.78 (0.05)	5.72 (0.05)	5.69 (0.05)	5.64 (0.05)	0.13
HDL cholesterol (mmol/l)	1.09 (0.01)	1.13 (0.01)	1.14 (0.01)	1.13 (0.01)	0.047
Total/HDL cholesterol	5.74 (0.08)	5.43 (0.08)	5.46 (0.08)	5.38 (0.08)	0.013
Triglyceride (mmol/l)*	1.83 (0.02)	1.66 (0.02)	1.64 (0.02)	1.60 (0.02)	0.0001
Fibrinogen (g/l)	3.80 (0.03)	3.79 (0.03)	3.76 (0.03)	3.70 (0.04)	0.012
FEV_1/height^2 (cl/m^2)	90.2 (1.0)	90.6 (1.0)	90.4 (1.0)	90.2 (1.0)	0.89
Insulin resistance* (HOMA)	1.47 (0.04)	1.25 (0.04)	1.21 (0.04)	1.21 (0.04)	0.0004
Non-manual social class (%)	22.2 (1.7)	28.0 (1.8)	37.3 (2.0)	40.7 (2.0)	0.0001
Father in non-manual social class (%)	8.4 (1.2)	10.7 (1.3)	11.7 (1.4)	18.5 (1.7)	0.0001
Father unemployed (%)	48.9 (2.3)	52.4 (2.3)	44.5 (2.3)	36.0 (2.2)	0.0001
Subject employed at baseline (%)	75.6 (1.7)	78.0 (1.7)	82.8 (1.5)	85.0 (1.5)	0.0001
Ever smoker (%)	82.5 (1.5)	86.3 (1.4)	84.1 (1.5)	83.5 (1.5)	0.82

*Geometric means, standard errors refer to logged data.

table 3. Blood pressure is not strongly related to any anthropometric measure while total cholesterol levels are inversely related to all the anthropometric measures. Lung function is positively related to both overall height and to trunk length, but not to leg length. Factors related to the insulin resistance syndrome—HOMA scores, triglyceride levels and total/HDL cholesterol ratio—are associated in opposite directions with leg and trunk length. Men with shorter legs are more liable to have high HOMA scores and high triglyceride levels while associations in the opposite direction are seen with trunk length. Height, on the other hand, tends to be unrelated to these measures.

All anthropometric measures are related to the occupational social class of the men, the occupational social class of the father's of the men and whether their fathers had been unemployed at any time during their childhood. Indicators of childhood socioeconomic circumstances were particularly strongly related to leg length. All anthropometric measures were positively related to the men being in employment. Smoking behaviour was unrelated to any of the anthropometric measures.

Risk of incident CHD in relation to the anthropometric measures, both before and after various adjustments for potential confounding or mediating factors, is detailed in

table 4. Leg length and leg length to trunk length ratio were both inversely associated with CHD risk. Adjustment for various potential confounding or intermediary factors had little influence on the effect estimates, although the level of significance was attentuated.

KEY POINTS
- Height is inversely related to CHD risk in many studies.
- We demonstrate that the inverse association is specific to leg length, and is not seen for trunk length.
- Leg length is also inversely associated with components of the insulin resistance syndrome, while trunk length is unrelated to these components.
- Leg length may serve as an indicator of exposures acting during childhood.

Discussion

Height has been inversely related to CHD risk in many studies[1–6 11 12 14 16 27] and a higher prevalence and greater severity of coronary atherosclerosis found at arteriography has also been reported among shorter men.[28] The weak and non-significant inverse association between overall height and incident CHD seen in this longer follow up of the Caerphilly Study represents an attenuation of the stronger inverse association seen over a five year follow up.[4] A similar decrease in the magnitude of the inverse association between height and CHD mortality with longer follow up has been seen in the Whitehall Study[16] and it was there postulated that this may reflect some of the height-CHD association being attributable to greater reductions in height occurring with aging among ill people. As the group of already sick people decreases in size because of selective mortality this group will have increasingly less influence on height-CHD incidence associations and the attenuation with follow up that is seen would be expected. While this may

Table 4 Odds ratios for CHD incidence for increase in one standard deviation of leg length, trunk length, height and leg length/trunk length ratio

	Leg length				
Variables in model	*Number of men with full data on variables considered*	*Unadjusted odds ratio for increase in leg length of one standard deviation**	*95% CI*	*Adjusted odds ratio for increase in leg length of one standard deviation**	*95% CI*
Anthropometric variables†	2427	0.90	[0.81, 1.00]	0.90	[0.80, 1.01]
CHD risk factors§§	2152	0.89	[0.79, 1.00]	0.94	[0.84, 1.06]
Insulin resistance¶¶	1904	0.88	[0.78, 0.99]	0.89	[0.79, 1.00]
Socioeconomic position***	2370	0.90	[0.81, 1.00]	0.91	[0.82, 1.02]
All listed variables†††	1771	0.87	[0.76, 0.99]	0.88	[0.76, 1.02]
	Trunk length				
Variables in model	*Number of men with full data on variables considered*	*Unadjusted odds ratio for increase in trunk length of one standard deviation‡*	*95% CI*	*Adjusted odds ratio for increase in trunk length of one standard deviation‡*	*95% CI*
Anthropometric variables§	2427	1.05	[0.94, 1.16]	1.07	[0.95, 1.20]
CHD risk factors§§	2152	1.04	[0.93, 1.17]	1.08	[0.96, 1.22]
Insulin resistance¶¶	1904	1.01	[0.89, 1.14]	0.98	[0.86, 1.10]
Socioeconomic position***	2370	1.06	[0.95, 1.18]	1.08	[0.96, 1.20]
All listed variables†††	1771	1.03	[0.91, 1.17]	1.12	[0.97, 1.30]
	Height				
Variables in model	*Number of men with full data on variables considered*	*Unadjusted odds ratio for increase in height of one standard deviation¶*	*95% CI*	*Adjusted odds ratio for increase in height of one standard deviation¶*	*95% CI*
Anthropometric variables**	2427	0.95	[0.86, 1.06]	1.05	[0.89, 1.23]
CHD risk factors§§	2152	0.94	[0.84, 1.06]	1.00	[0.88, 1.12]
Insulin resistance¶¶	1904	0.92	[0.81, 1.04]	0.91	[0.80, 1.03]
Socioeconomic position***	2370	0.96	[0.86, 1.07]	0.98	[0.87, 1.09]
All listed variables†††	1771	0.92	[0.81, 1.05]	1.12	[0.91, 1.36]
	Leg length/trunk length ratio				
Variables in model	*Number of men with full data on variables considered*	*Unadjusted odds ratio for increase in leg length/trunk length ratio of one standard deviation††*	*95% CI*	*Adjusted odds ratio for increase in leg length/trunk length ratio of one standard deviation††*	*95% CI*
Anthropometric variables‡‡	2427	0.88	[0.80, 0.98]	0.88	[0.75, 1.03]
CHD risk factors§§	2152	0.87	[0.77, 0.98]	0.92	[0.81, 1.03]
Insulin resistance¶¶	1904	0.87	[0.77, 0.98]	0.89	[0.79, 1.01]
Socioeconomic position***	2370	0.88	[0.79, 0.98]	0.89	[0.80, 1.00]
All listed variables†††	1771	0.86	[0.75, 0.97]	0.83	[0.68, 1.01]

*Odds ratio for increase in leg length of one standard deviation (4.4 cm), adjusted for age. †Anthropometric variables in the model: trunk length. ‡Odds ratio for increase in sitting height of one standard deviation (3.3 cm), adjusted for age. §Anthropometric variables in the model: leg length. ¶Odds ratio for increase in height of one standard deviation (6.5 cm), adjusted for age. **Anthropometric variables in the model: sitting height. ††Odds ratio for increase in leg length/trunk length ratios of one standard deviation (3.3 cm), adjusted for age. ‡‡Anthropometric variables in the model: height. §§CHD risk factors in the model: BMI, FEV/H^2, cholesterol, fibrinogen, diastolic blood pressure, ever smoked, currently smoke. ¶¶Insulin resistance factors in the model: HOMA, log triglycerides, HDL cholesterol. ***Indicators of socioeconomic position in the model: own social class, father's social class (including a category for not known), father unemployed (including a category for not known). †††All variables from all four categories entered in the model.

contribute to the association between overall height and CHD being weaker at this longer follow up in the Caerphilly Study, it is unlikely to account for an inverse association between leg length and CHD incidence. Longitudinal studies examining reductions in height with age suggest that this occurs preferentially in trunk rather than leg component of total height, probably due both to shrinkage in the vertebral column and scoliosis.[29] Thus associations between leg length, which is less affected by aging, and CHD incidence are unlikely to be confounded by adult disease processes leading to shrinkage in those with ill health.[16]

The specific association of leg length and CHD incidence has implications for other potential mechanisms linking height and CHD risk. In this study we see that trunk length, rather than leg length, is positively associated with lung function. This is the expectation that follows from simple mechanical considerations. If the association between height and CHD risk were mediated through lung function, as has been suggested,[14] it would be expected that trunk length, rather than leg length, would be the important component of total height. The fact that the reverse is the case suggests that the lung function hypothesis cannot provide a full explanation of the association between height and CHD risk. Inhibited fetal development, reflected in lower height in adulthood, has been advanced to explain the association between height and CHD. The hypothesis here is that it is poor fetal development that is the fundamental causal factor, and height serves as a marker of this. However, the correlations between birth weight, the indicator of fetal development used in many of the prospective studies investigating the fetal origins of CHD, and the two components of height are similar, r=0.17 for trunk length and r=0.12 for leg length—in this study. Data from other studies also demonstrate similar correlations of birth weight (and birth weight adjusted for birth length) with trunk length and leg length.[30] If impaired fetal development underlay the height-CHD associations it would be expected that both components of height would have similar associations with CHD. Again this is counter to the results we obtained.

Leg length seems to serve as an indicator of nutritional status in childhood.[31] It is the component of overall height that grows proportionately more in the years up to puberty,[32] as shown by changes in the sitting height: height ratio from birth to adulthood from around 0.66 to around 0.52[33] and secular increases in height are thought to be largely attributable to leg length increases.[34] Thus, in the observed relations between leg length and CHD mortality, leg length may be acting as a sensitive marker for environmental exposures in childhood leading both to growth retardation and later predisposition to CHD.

Other explanations for the height-CHD relation may be classified under two headings—confounding and mechanical. Height-CHD relations may be confounded by adult risk factors. For example, children exposed to environmental factors that retard growth may be more likely to become adult smokers[35]; similarly, taller children are more likely to experience upward social mobility[36] and adults in upper socioeconomic groups are at reduced CHD risk. Adjustment for both adult risk factors and social class partially attenuated some of the hazard ratios seen in our analyses. Attenuation with respect to adult risk factors may be because alterations of these are the mechanism through which childhood exposures affect adult CHD risk. Thus, rather than adjusting for a confounding factor, one is adjusting for a risk factor lying on the causal pathway of the observed associations, thereby diminishing "true" effects. Mechanical explanations suggest that reduced stature is associated with diminished coronary artery lumen diameter and thereby greater risk of occlusion.[15] If this explanation were valid, one might expect to see stronger relations with trunk length, as this may more directly relate to body mass and hence heart and coronary size. This was not found in our analyses.

Height in adulthood has been inversely associated with the risk of adult onset diabetes and impaired glucose tolerance in some[37 38 39] but not all[40] previous studies. This association could reflect common genetic factors influencing both height and later glucose tolerance; intrauterine development and its associations with adulthood height and later glucose tolerance, or childhood circumstances that influence final attained height and later glucose tolerance. Evidence that the inverse association between height and glucose tolerance is independent of birth weight has been interpreted as indicating that the association does not simply reflect the influence of intrauterine environment. In our analyses we demonstrate clearly that the association between stature and insulin resistance—together with other components of the metabolic syndrome, including triglyceride levels and obesity—are linked specifically to leg length. As birth weight is similarly associated with height, with leg length and trunk length, the specific associations between leg length and components of the metabolic syndrome are unlikely to reflect the common influence of intrauterine development, which is reflected in birth weight. However, the relevance of insulin resistance[41] and the components of the metabolic syndrome for subsequent development of CHD have been questioned among non-diabetics.[42] Statistical adjustment for components of the insulin resistance syndrome did not greatly attenuate the association between leg length and incident CHD. Thus it seems that additional mechanisms link leg length to risk of CHD.

Adverse social circumstances in childhood are related to increased risk of CHD mortality,[43] and to components of the metabolic syndrome.[44] Leg length and leg length to trunk length ratio, both in childhood and in adulthood, may reflect the influence of growth patterns, which, in turn influence later disease risk. In both this study and in the Boyd Orr cohort—in which leg length was measured in childhood—the association between components of stature and adult disease risk were statistically independent of socioeconomic indicators in both childhood and in adulthood. Thus

the leg length association with adulthood disease does not appear to simply reflect confounding by social circumstances.

Leg length and leg length to trunk length ratio in adulthood seem to be influenced by factors constraining early childhood growth (poorer socioeconomic circumstances result in shorter legs and a lower leg length to trunk length ratio), however later puberty (which may also reflect adverse circumstances) results in greater leg length to trunk length ratios.[45] Thus leg length and leg to trunk length ratio in adulthood will be a less useful indicator of childhood circumstances than leg length measured in childhood. This may explain why the associations with CHD were of greater magnitude in the Boyd Orr cohort, in which anthropometric measurements were taken in childhood, than in this study.[13]

In conclusion, leg length is inversely associated with the risk of CHD and with components of the insulin resistance syndrome among adults. This provides supportive evidence for the hypothesis that impaired growth during childhood increases the risk of these conditions. The finding should, however, be considered in the light of evidence suggesting that high calorie intake in childhood, longer legs in childhood and greater final achieved stature are associated with an increased risk of non-smoking relating cancers.[6 16 19 46] Further research is required to delineate the overall influence of encouraged growth in childhood on adult health.

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